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# The Effects of Essential Fatty Acid Supplementation by Efamol in Hyperactive Children

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*Thirty-one children, selected for marked inattention and overactivity, were studied in a double-blind, placebo-controlled crossover study of essential fatty acid (EFA) supplementation. Subjects received the active treatment and placebo conditions for 4 weeks each and were assessed on a variety of cognitive, motor, and standardized rating scale measures. EFA supplementation (evening primrose oil; Efamol® ) resulted in significantly lower levels of palmitoleic acid (a nonessential fatty acid) and higher concentrations of dihomogammalinolenic acid, an EFA previously found to be deficient in some hyperactive children. Supplementation was also associated with significant changes on two performance tasks and with significant improvement to parent ratings on the subscales designated as Attention Problem and Motor Excess of the Revised Behavior Problem Checklist. However, a variety of eight other psychomotor performance tests and two standardized teacher rating scales failed to indicate treatment effects. When the experimentwise probability level was set at .05, only 2 of 42 variables showed treatment effects. Baseline EFA concentrations appeared to be unrelated to treatment response. It was concluded that EFA supplementation, as employed here, produces minimal or no improvements in hyperactive children selected without regard to baseline EFA concentrations.*

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Recently there has been interest in the possibility that deficient levels of essential fatty acids (EFAs), the precursors of prostaglandins, may be linked to the presence of hyperactivity in some children. Colquhoun and Bunday (1981) have examined the literature on hyperactivity, and they suggested that many hyperactive children may have a deficiency of EFAs because of (a) inability to metabolize linoleic acid normally or (b) difficulty absorbing EFAs normally from the intestine or (c) EFA requirements that are higher than normal. These conclusions were reached following a survey of children belonging to the Hyperactive Children's Support Group in England. First, Colquhoun and Bunday noted that the majority of children in this organization had a history of atopic disorders, which are known to respond to EFA supplementation. Second, thirst (which is an early feature of EFA deficiency in animals) was frequently reported as a symptom of these children by their parents. Third, Colquhoun and Bunday observed that male animals require about three times as much EFAs as females for normal development. This was considered suggestive because of the high ratio of boys to girls (at least 3 to 1) in most studies of hyperactivity. Fourth, certain dietary substances have been implicated by some workers (e.g., Feingold, 1975) as adversely affecting the behavior of hyperactive children. A number of these substances (tartrazine and salicylates) are known to be weak inhibitors of conversion of EFAs to prostaglandins (Horrobin, 1981). Colquhoun and Bunday (1981) also reported anecdotally that about 25 children in their organization had received an EFA supplement for their hyperactivity and that at least half had responded positively.

Mitchell, Lewis, and Cutler (1983) compared EFA profiles in an amorphous group of "maladjusted" (including many who could have been classified as hyperactive) children with a control group. None of the differences on individual EFAs distinguished the groups at statistically significant levels. However, a multivariate analysis incorporating five of the EFAs showed a highly significant difference between the groups and this difference was particularly evident in respect to the fatty acids of the n-6 metabolic pathway.

More recently, we carried out a comparison of 47 children rated as highly inattentive both by their parents and by their teachers and 45 age-and sex-matched controls (Mitchell, Aman, Turbott, & Manku, 1986). The inattentive (i.e., hyperactive) group was found to have significantly lower levels of docosahexaenoic (22:6n-3), dihomogammalinolenic (20: 3n-6), and arachidonic (20:4n-6) acids. In agreement with Colquhoun and Bunday's (1981) observation, more hyperactive children in our study were reported to drink unusual quantities of fluids (parent reports) than was the case for control children. However, unlike Colquhoun and Bunday, we found no evidence of a greater prevalence of atopic disorders (e.g., asthma, eczema) among the hyperactive children themselves or their relatives.

Thus, there are both theoretical and empirical reasons for considering EFA supplementation as a possible treatment for hyperactive children. So far, group comparisons have been somewhat inconsistent in their findings, but there has been a recurring suggestion that deficiencies in EFA levels may exist in a subgroup of children considered to be hyperactive. It is likely that some of the inconsistencies reported thus far have been due to differences in subject selection procedures across studies. The present study was conducted to evaluate the effects of an EFA supplement (Efamol® ; oral evening primrose oil) on the behavior, learning, and motor performance of a group of children selected for problems of inattention and hyperactivity.

## METHOD

### *Subjects*

Prior to entry into the study, prospective subjects were rated by their parents on the Revised Behavior Problem Checklist (RBPC; Quay, 1983) and by their teachers on the Conners (1969) Teacher Questionnaire. Two criteria were employed for selecting subjects. First, children were admitted to the study if their scores on *both* the Attention Problem subscale (III) of the RBPC and the Inattention subscale (II) of the Teacher Questionnaire exceeded the 90th percentile using normative data from Auckland children (Aman, Werry, Fitzpatrick, Lowe, & Waters, 1983; Werry & Hawthorne, 1976). Twenty-six (84%) of the children were included by this rule. Five additional children were seen by a child psychiatrist as part of another study (Reeves, Werry, Elkind, & Zametkin, in press). As these children were given a diagnosis of Attention Deficit Disorder (either with or without Hyperactivity) (DSM-III; American Psychiatric Association, 1980), they were also admitted to the study. Of these five subjects, it is noteworthy that four exceeded the 90th percentile on both the Motor Excess and Hyperactivity subscales (but not necessarily the subscales related to attention problems) of the RBPC and the Teacher Questionnaire.

The definitive group comprised 4 girls and 27 boys. Other characteristics of the group are summarized in Table I. These children received generally high ratings on most subscales of the RBPC, a point that will be discussed later. Most noteworthy, however, are the obtained scores relating to attention difficulties on the two rating scales. Upon entry to the study, the subjects had mean standardized scores of 5.05 on the Attention Problem subscale of the RBPC and 2.45 on the Inattention subscale of the Teacher Questionnaire. Thus, as a group, these children were consistently perceived as having attention deficits both in the home and in the classroom.

Before entry into the study, the senior author conducted a semistructured interview about the developmental history and current status of the children. Six had a history of febrile convulsions and one of these subsequently developed epilepsy that was resolved by the time of the study. However, none of the children were known to have neurological disorders and none were receiving medication at the time of the study, although a minority were on various diets intended to reduce hyperactivity. None of the children were frankly mentally retarded, although two had IQs falling in the borderline range (< 75 on the Peabody Picture Vocabulary Test). Severe inattention, impulsivity, and (usually) overactivity were longstanding problems for all children, typically dating from early childhood, and of greater than a year's duration in all cases.

### *Design*

A double-blind, placebo-controlled crossover design was used. Each child consumed three capsules, twice daily, containing either essential fatty acid supplementation (Efamol) or placebo. Each Efamol capsule contained 360 mg of linoleic acid and 45 mg of gamma-linoleic acid, and the indistinguishable placebo capsules each contained 500 mg of liquid paraffin. This dosage (i.e., 6 capsules/day) generally exceeded levels claimed by others to have behavioral effects (Colquhoun & Bunday, 1981) or shown to be effective in treating atopic eczema (Wright & Burton, 1982). Subjects were tested five times each: once prior to treatment (pretest) and at 2 and 4 weeks within each treatment phase. A washout period of at least 1 week intervened between the Efamol and placebo conditions. A random half of the subjects received placebo for the first 4 weeks, followed by 4 weeks of Efamol, whereas the remaining children received the alternative order of treatment.

At the pretest and at the end of each 4-week treatment phase, 10-ml blood samples were taken. This was done to determine whether initial EFA concentrations were related to clinical response and to see whether supplementation resulted in measurable changes to EFA levels.

### *Procedure*

Approval for the study was obtained from the Ethical Committee of the Auckland Medical School, and informed, written consent was obtained from the parents of all participants. At each 2-week assessment interval, the children were brought to the laboratory for evaluation on a psychomotor

test battery. Thus, the children were assessed in a pretest and twice during the Efamol and placebo phases.

*Cognitive and Motor Tests.* Most of these tests were controlled by electronic equipment that automatically presented stimuli, recorded responses and response times, and (during the cognitive tasks) provided feedback to the subjects about the correctness of each response. The majority of the tests were selected to assess various aspects of attention or distractibility because of the widespread belief today that attentional problems are central to the disorder (Aman, 1984). Furthermore, many of the tests within the battery have been shown to be sensitive to a variety of psychotropic drugs, including methylphenidate and haloperidol (Werry & Aman, 1975) and imipramine (Werry, Aman, & Diamond, 1980). The following learning and motor performance measures were included in the battery.

1. Matching Familiar Figures Task (Automated; Kagan, 1965). In our modified version of this task, the child was required to select from among four line drawings the one that matched a standard that was presented at the top of the display. The task is widely regarded as a test of impulsivity and visual analysis skills. Both the Preschool and Elementary versions were used, for a total of 24 trials. Accuracy and response time for each trial were measured.

2. Short Term Memory Task (Automated; Sprague & Sleator, 1977; Werry & Aman, 1975). In this task, the child was shown 10 arrays each of three or nine pictures, followed by a single test picture. The subject had to decide whether the test picture was or was not contained in the previous array by depressing a "Same" or a "Different" response lever. Accuracy and response time were recorded for each response.

3. Memory Distraction Task (Automated). This task involved the presentation of block patterns similar to the Block Designs test in the Wechsler (1974) Intelligence Scale for Children. Four seconds after display of this stimulus, the subject was shown an array of four designs, one of which was identical to the original pattern, and the subject was required to press a button corresponding to the correct pattern. During half of the trials, there was a series of novel and interesting pictures scattered around the original stimulus, as well as the test designs. Our intention was to test these children for memory under both distracting and nondistracting conditions. There were 16 trials each under the distracting and the nondistracting condition. Accuracy and response time were analyzed separately for these two conditions.

4. Continuous Performance Task (Automated). This task, originally developed by Rosvold, Mirsky, Sarason, Bransome, and Beck (1956), is widely regarded as a useful measure of attention span and is frequently employed in drug research with children (Aman, 1978). In our version of

the task, the child was required to respond whenever the target letter (*X*) was displayed and to refrain from responding when the alternative letter (*C*) was illuminated (Aman & Wakeman, 1981). The letters were displayed randomly for .3-sec intervals over a 10-minute period, and the child had 2.5 seconds in which to respond to each target. Three measures were recorded: failures to detect the target (omission errors), responses to the nontarget (commission errors), and response time.

5. Seat Movements (Automated). During each of the above tasks, seat activity was recorded using a stabillometric seat developed by Sprague and Toppe (1966). All seat activity, except that occurring in the variable response intervals, was automatically recorded without the subject's knowledge.

6. Component Selection Task (Hale & Morgan, 1973; Hale & Taweel, 1974). In this task, the subject was required to learn the serial position of six stimuli on a form board. In our modification of this task, each stimulus was made of up three components—namely, a unique geometric shape and color, on which was superimposed the line drawing of an animal. The form board was equipped with a hinged flap that was used to conceal the stimuli during test trials. Serial position was tested by randomly presenting each stimulus above the form board, and the subject was required to indicate the position judged to be correct. The children were required to learn the position of each stimulus to criterion, defined as two consecutive trials without error. This constituted the central learning part of the task. After the criterion was reached, the children were tested for their memory of the individual components. This was done by closing the flap and presenting attributes of each dimension—for example, a colorless square, a red card, or a drawing of a butterfly. The subject indicated his or her response by touching the position on the form board corresponding to that stimulus during learning. As there were six complex stimuli, it was possible to test for a total of 18 stimulus components. This measure, number of components recalled, provided an index of incidental learning. Two dependent variables were analyzed: errors to criterion during the serial learning phase (denoting central learning), and number of components correctly recalled during the posttesting phase (incidental learning).

7. Cancellation Task. This was a subject-paced vigilance-type task. Geometric figures were printed randomly in rows on test sheets and the subject was required to scan these, as quickly as possible, and cross out all the squares. The task was timed for each sheet so that there was insufficient time to cancel out all the targets presented. Around the periphery of each sheet was a series of five pictures (cartoon characters and storybook figures). Nothing was said about these until all four of the test sheets had been administered. The child was then tested on the distraction material,

which had appeared in the margins. This was done by presenting the subject with a test booklet containing 20 pages. Each page contained four pictures, one of which had appeared previously in the margins of the test sheets. The subject was asked to identify which of the four pictures he or she had seen before.

The central (cancellation) task was used as a measure of attention span, whereas the subsequent identification of peripheral pictures served as an operational measure of the extent of distraction that had occurred. Three measures were collected during performance of the cancellation task: number of correct detections, missed targets (omission errors), and geometric figures that were incorrectly canceled (commission errors). During posttesting, the number of pictures correctly identified was also recorded. A previous study with this task has shown that both omission and commission errors discriminate between hyperactive and control subjects (Aman & Turbott, 1986).

8. Motor Steadiness Tests (Automated). These were adapted from Klove's (1963) Motor Steadiness Battery. During the Maze test, the child was required to run a stylus through a maze while trying not to touch the sides. In the Graduated Holes test, the child was required to hold the stylus in the center of a series of five holes, increasingly smaller in size and for 10 seconds each, without touching the sides. Two variables were electronically recorded for each test: number of errors (summed over both hands) and total error time.

9. Pursuit Rotor Task (Automated). This employed a converted phonograph turntable that rotated at 16 RPMs and projected a photobeam upward, through a plate of glass. The child was asked to track the beam with a probe, fitted with a photocell, and three trials with each hand were allowed. The dependent measure was total contact time, summed over both hands.

*Rating Scale Measures.* At the end of each 2 week interval, the subjects were rated on the following instruments.

1. Parents rated the children on the Revised Behavior Problem Checklist (RBPC; Quay, 1983), which is a factor-analytically derived scale rendering six subscales: (I) Conduct Problem, (II) Socialized Aggression, (III) Attention Problem, (IV) Anxiety-Withdrawal, (V) Psychotic Behavior, and (VI) Motor Excess. The scale has been shown to be factorially valid for New Zealand children (Aman et al., 1983) and to discriminate clinic attenders from nonattenders (Aman & Werry, 1984).

2. Teachers rated the children on the Conners (1969) Teacher Questionnaire, another empirically derived checklist, which resolves into four subscales: (I) Conduct Problem, (II) Inattention, (III) Tension/Anxiety, and (IV) Hyperactivity.

**Table I.** Subject Characteristics[a]

| Variable | *Mean* | | *SD* | |
|---|---|---|---|---|
| Age (years) | 8.86 | | 1.88 | |
| IQ (Peabody Picture Vocabulary Test) | 101.07 | | 16.34 | |
| Teacher Questionnaire | | | | |
| I. Conduct problem | 1.69 | (1.58) | .66 | (.52) |
| II. Inattentive/passive | 3.08 | (1.93) | .62 | (.60) |
| III. Tension/anxiety | 1.70 | (1.63) | .62 | (.47) |
| IV. Hyperactivity | 2.80 | (2.01) | .80 | (.72) |
| Revised Behavior Problem Checklist | | | | |
| I. Conduct problem | 23.23 | (5.06) | 10.48 | (6.52) |
| II. Socialized aggression | 3.71 | (.58) | 4.41 | (1.40) |
| III. Attention problem | 20.42 | (2.79) | 5.32 | (4.46) |
| IV. Anxiety/withdrawal | 9.13 | (2.92) | 5.82 | (3.36) |
| V. Psychotic behavior | 3.52 | (.43) | 3.10 | (.99) |
| VI. Motor excess | 6.23 | (.97) | 2.14 | (1.43) |

[a]Normative values, prorated by sex, appear in parentheses (from Werry & Hawthorne, 1976, and Aman et al., 1983, respectively).

3. Teachers were also asked to complete the ADD-H: Comprehensive Teacher Rating Scale (ACTeRS; Ullmann, Sleator, & Sprague, 1984). Also a factor-analytically derived scale, this instrument was specifically developed to assess hyperactivity, and it has four subscales, as follows: (I) Attention, (II) Hyperactivity, (III) Social Skills, and (IV) Oppositional Behavior.

*Side Effects.* Subjects were assessed at each visit using the Dosage and Treatment Emergent Symptoms Scale (DOTES; Guy, 1976). This is a standardized scale developed by the National Institute of Mental Health for assessing side effects of pharmacotherapy.

## RESULTS

### *Serum EFA Concentrations*

Serum essential fatty acid levels were determined, without knowledge of treatment condition, using the method described by Manku, Horrobin, Huang, and Morse (1983). EFA concentrations were then statistically analyzed as a function of Drug Order and Treatment condition (repeated measures). The results, presented in Table II, indicated that there was a significant *reduction* in concentrations of palmitoleic acid (16:1n-7) during treatment with Efamol and a significant increase in the levels of dihomogammalinolenic acid (20:3n-6). The change in dihomogammalinolenic acid during treatment amounted to a 14% increase over the placebo levels, which surpassed control group values in our other study

**Table II.** Effect of Supplementation on Fatty Acid Serum Concentrations

| Variable | | Placebo | Efamol | *F* |
|---|---|---|---|---|
| Palmitic | 16:0 | 26.88 | 26.78 | .32 |
| Palmitoleic | 16:1n-7 | 1.80 | 1.63 | 6.21[b] |
| Stearic | 18:0 | 11.40 | 11.59 | .20 |
| Oleic | 18:1n-9 | 12.50 | 11.94 | 3.38 |
| n-3 series | | | | |
| Alpha-linolenic | 18:3n-3 | .37 | .24 | 3.48[d] |
| Eicosapentaenoic | 20:5n-3 | 1.10 | 1.11 | .01 |
| Docosatetraenoic | 22:4n-3 | .39 | .44 | .77 |
| Docosohexaenoic | 22:6n-3 | 3.02 | 3.11 | .25 |
| n-6 series | | | | |
| Linoleic | 18:2n-6 | 26.49 | 27.16 | .78 |
| Gamma-linolenic | 18:3n-6 | .053 | .031 | .46 |
| Dihomogammalinolenic | 20:3n-6 | 2.58 | 2.93 | 7.38[c] |
| Arachidonic | 20:4n-6 | 8.59 | 8.59 | 0 |
| Docosapentaenoic | 22:5n-6 | .29 | .24 | .96 |

[a]Values are mean percentages of the fatty acids in the phospholipid fraction. Drug Order and Drug Order by Treatment effects were all nonsignificant, except for docosahexaenoic acid, where there was a significant Drug Order effect ($p < .007$).
[b]$p < .02$.
[c]$p < .01$.
[d]$p < .07$.

(Mitchell et al., 1986). The remaining EFAs showed no changes, although there was a nonsignificant tendency for alpha-linolenic acid (18:3n-3) to decrease during the treatment phase.

### *Psychomotor Tests and Rating Scales*

The data were analyzed using a statistical package called GENSTAT (Alvey et al., 1977). An analysis of covariance model was used, where time served at the covariate and Treatment condition (repeated measures) was crossed with Drug Order. This corrected for practice due to successive testing on the various tasks and eliminated the possibility of practice effects being confounded with drug effects. Several of the variables were markedly skewed to the right. In the case of the Continuous Performance Task and seat activity, the raw data were transformed by converting raw scores to square roots. The remaining variables requiring transformation were converted by log transformations. In no case did this result in a nonsignificant variable becoming statistically significant. For the automated tests, both response time and its reciprocal, speed, were analyzed. Only the measure showing the stronger treatment effect is summarized here. Again, this did not result in any instances of a nonsignificant variable becoming "significant."

**Table III.** Summary for the Main Effect of EFA Supplementation

| Variable | Placebo | Efamol | *F* |
|---|---|---|---|
| Matching Familiar Figures | | | |
| Accuracy (%) | 77.46 | 77.50 | .001 |
| Response speed (1/sec) | .174 | .171 | .199 |
| Seat movement[a] | 38.00 | 39.10 | .372 |
| Short Term Memory | | | |
| Accuracy (%) | 77.00 | 80.10 | 4.456[e] |
| Response time (sec)[b] | 2.74 | 2.62 | .830 |
| Seat movements[a] | 70.00 | 63.20 | .646 |
| Memory Distraction Task | | | |
| (Nondistracting condition) | | | |
| Accuracy (%) | 64.79 | 64.88 | .002 |
| Response time (sec) | 5.97 | 5.93 | .019 |
| (Distracting condition) | | | |
| Accuracy (%) | 61.90 | 62.00 | .004 |
| Response time (sec)[b] | 7.39 | 10.11 | 17.512[f] |
| Seat movement[a] (total, both conditions) | 102.40 | 97.90 | .190 |
| Continuous Performance Task | | | |
| Omission errors[a] | 6.84 | 8.10 | .774 |
| Commission errors[a] | 7.43 | 6.36 | .832 |
| Response speed (1/sec)[b] | 1.118 | 1.078 | 1.353 |
| Seat movements[a] | 74.50 | 70.20 | .471 |
| Component Selection Task | | | |
| Errors to criterion[a] [87][c] | 4.65 | 4.53 | .004 |
| Total recalled | 11.73 | 12.01 | .384 |
| Cancellation Task | | | |
| Correct Detections [87] | 265.10 | 264.40 | .045 |
| Omission errors[a] [87] | 2.80 | 2.40 | .126 |
| Commission errors[a] [88] | 1.63 | 2.08 | .426 |
| Incidental pictures identified [87] | 7.31 | 7.60 | .411 |
| Maze Task | | | |
| Number of contacts | 41.56 | 43.75 | 1.960 |
| Contact time (sec)[b] | 5.48 | 5.59 | .009 |
| Graduated Holes Task | | | |
| Number of contacts | 164.60 | 172.80 | 2.619 |
| Contact time (sec) | 29.68 | 29.86 | .032 |
| Pursuit Rotor Task | | | |
| Contact time (sec) | 36.99 | 37.69 | 1.195 |
| Revised Behavior Problem Checklist | | | |
| I) Conduct problem [88] | 17.61 | 16.30 | 2.364 |
| II) Socialized aggression [88] | 1.18 | 1.26 | .151 |
| III) Attention problem [88] | 17.37 | 14.97 | 16.002[f] |
| IV) Anxiety-withdrawal [88] | 5.73 | 6.06 | .677 |
| V) Psychotic Behavior [88] | 2.02 | 1.62 | 2.730 |
| VI) Motor excess [88] | 5.05 | 4.48 | 5.746[e] |

**Table III.** Continued

| Variable | Placebo | Efamol | $F$ |
|---|---|---|---|
| Conners Teacher Questionnaire | | | |
| I) Conduct problem [76] | 1.66 | 1.62 | .482 |
| II) Inattention [76] | 2.66 | 2.69 | .155 |
| III) Tension anxiety [76] | 1.70 | 1.73 | .446 |
| IV) Hyperactivity [76] | 2.58 | 2.58 | .005 |
| ACTeRS | | | |
| Attention [75] | 13.26 | 13.37 | .050 |
| Hyperactivity [75] | 16.51 | 16.91 | 1.119 |
| Social skills [74] | 19.15 | 18.93 | .290 |
| Oppositional [74] | 14.95 | 14.18 | 2.604 |
| Global 1 (acceptance by peers) [74] | 4.96 | 4.86 | .201 |
| Global 2 (requires teacher time) [74] | 6.32 | 6.66 | 3.604[d] |

[a]Square root transformation used.
[b]Log transformation used.
[c]Degrees of freedom = 1,90 for all variables except those with brackets, where $n_2$ is shown. For ease of interpretation, means of raw scores are shown here, even when transformations were used to calculate $F$ values.
[d]$p < .10$.
[e]$p < .05$.
[f]$p < .001$.

The results are summarized for the main effect of treatment (EFA supplementation) in Table III. As is clear from the table, only a small minority of mesures showed treatment-related changes. Accuracy was significantly improved as a result of Efamol on the Short Term Memory Task. EFA supplementation was associated with a substantial increase in response time during the distraction condition on the Memory Distraction Task, but it is unclear whether this should be regarded as evidence of improvement or deterioration. Parents reported significantly fewer problems on the Attention Problem and Motor Excess subscales during the Efamol phase. However, similar types of change were not reported by teachers on the Conners Teacher Questionnaire. On the ACTeRS Global 2 dimension, relating to "requirements for teacher's time," Efamol resulted in perceptions of nonsignificantly ($p < .10$) greater demands on the teacher.

It should be noted that a large number (42) of behavioral measures were used to monitor drug effects. If the experimentwise alpha probability is set at the .05 level, then the required probability for each variable to reach significance would be .0012. Only two variables, response time on the distraction task and parent ratings of attention problems, exceeded this level. Thus, although there were some suggestions of therapeutic changes,

the large majority of measures failed to show an effect due to EFA supplementation when this more rigorous criterion is applied.

### *Subgroup Analysis—Baseline EFA Levels and Treatment Response*

Of course, it may be inappropriate to predict uniform improvements in this heterogeneous group of children, since only a minority would be expected to be markedly deficient in EFA levels. Therefore, we conducted another set of analyses to evaluate response in terms of baseline levels on three fatty acids. As our previous study (Mitchell et al., 1986) showed significant differences between hyperactive and control subjects on docosahexaenoic, dihomogammalinolenic, and arachidonic acids, the present group was subdivided according to baseline levels on these three EFAs. An analysis of covariance model was again used as described earlier, analyzing for the effects of Drug Order and Treatment and controlling for Time. However, a third independent variable (Baseline level) was introduced in which the subjects were subdivided according to whether they had low or high serum levels on these three fatty acids before the study began.

In the case of docosahexaenoic acid, there were three variables having significant interactions between Drug and Subgroup. However, changes on two of these were contrary to the prediction that subjects who were initially low on docosahexaenoic acid would show a more favorable response to EFA supplementation. For dihomogammalinolenic acid, six variables showed significant Drug by Subgroup interactions. On four of these, however, the subjects with the lowest baseline concentrations responded more poorly to treatment, again challenging the hypothesis under study. None of the analyses based on arachidonic acid levels revealed subgroup interactions. Thus, it cannot easily be argued that there was a differential response determined by subjects' baseline fatty acid levels and that therapeutic changes were merely obscured by heterogeneity in the group.

### *Side Effects*

The only significant and unequivocal side effect to appear during the trial occurred in a boy who previously was given a questionable diagnosis of pancreatic enzyme deficiency. This boy, who had been assigned to the placebo-Efamol sequence, developed severe diarrhea on three separate occassions when placebo treatment was attempted. As a result, he never completed the trial and he was not included in the group of subjects described earlier.

## DISCUSSION

As noted earlier, there was a tendency for parents to rate these children somewhat high on all dimensions of the RBPC, raising questions about the extent to which the subjects were truly hyperactive. However, a dual criterion of high inattention scores on *both* the RBPC and the Teacher Questionnaire was imposed for the large majority of subjects. Whereas the parents were rather nonspecific in their perceptions of these children, ratings by the teachers were consistently high for only one subscale—namely Inattention. Furthermore, the interview confirmed that the most salient features of these children were inattention, impulsivity, and (usually) overactivity, and the vast majority of subjects had these symptoms from infancy or early childhood. Thus, the high overall ratings on the RBPC appear to reflect what O'Leary (1981) has called a "halo error" or what Milich, Loney, and Landau (1982) have referred to as "source problems." However, evaluations from a variety of sources (parents, teachers, and interviewer) were consistent with the picture of hyperactivity.

The rationale for employing EFA supplementation with hyperactive children appears reasonable on the basis of clinical characteristics and previous work suggesting EFA deficiencies in these children (Colquhoun & Bunday, 1981; Mitchell et al., 1983, 1986). However, it must be concluded that EFA supplementation, employed with hyperactive children unselected for baseline EFA concentrations and treated at the present dosage, had relatively few clinical or cognitive effects. Two children each were found to improve to at least a moderate degree during the placebo and Efamol treatment phases, and we are aware of only one family (whose child was not among the "improvers") that elected to continue Efamol treatment after the study. Certainly our findings bore no resemblance to the 50% rate of improvement reported in the uncontrolled trial carried out by Coloquhoun and Bunday (1981). Indeed, when the experimentwise probability level was set at .05, only 2 of the 42 variables showed significant changes, and the nature of one of these (i.e., improvement vs. worsening) is difficult to interpret.

The subgroup analyses that took into account the baseline levels of the subjects on docosahexaenoic, dihomogammalinolenic, and arachidonic acids failed to indicate a differential response for individuals who were initially low or high on these substances. This also is damaging to the hypothesis that EFA supplementation is a viable treatment for hyperactive children, since it would be predicted from this model that subjects with initially low concentrations of EFAs would show the greatest clinical response. Nor can it be argued that the dose assessed here was inap-

propriate. Our dose corresponded to the largest level used by Colquhoun and Bunday (1981), and it was larger than the dose used successfully to treat atopic eczema in another group of children (Wright & Burton, 1982). Furthermore, it equaled the maximum starting dose recommended for children by the company that manufactures Efamol.

The data on changes in EFA levels indicate that we were at least partially successful in altering EFA concentration, as witnessed by a significant increase in concentrations of dihomogammalinolenic acid (20:3n-6). The 14% increase observed here actually brought the treatment mean for this group up to the level of the control group in our earlier comparison study (Mitchell et al., 1986). Our results provided only minimal support for this particular form of treatment (i.e., Efamol monotherapy, in this dose), but this does not wholly discredit the EFA deficiency *hypothesis* of hyperactivity or related forms of treatment. Although dihomogammalinolenic acid levels were normalized in terms of serum concentration, it is possible that there were still deficiencies at the cellular level. Furthermore, arachidonic acid concentrations for the present group ($M$ = 8.59%) were even lower than for the hyperactive children in our previous study ($M$ = 9.26%), where the differences from control values ($M$ = 9.88%) were significant. As the levels of arachidonic acid were unchanged as a function of Efamol treatment, it is possible that the metabolism of arachidonic acid from dihomogammalinolenic acid was limited by deficiencies in the enzyme concerned with this metabolic step—namely, delta-5-desaturase. Thus, in further studies of the utility of EFA supplementation for hyperactivity, it may be profitable to consider administering arachidonic acid in conjunction with dihomogammalinolenic acid precursors. However, notwithstanding these possibilities, the burden of proof lies with those who would advocate this form of therapy first to establish its efficacy before claiming that it has a therapeutic role to play in treating hyperactive children.

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